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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,094	07/17/2003	Remy Gross	0160.00	1055

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NEKTAR THERAPEUTICS
150 INDUSTRIAL ROAD
SAN CARLOS, CA 94070

EXAMINER	
ROGERS, JAMES WILLIAM	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,094	GROSS ET AL.	
	Examiner	Art Unit	
	James W. Rogers, Ph.D.	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☒ Claim(s) *18,20 and 22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/10/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 18,20,22-25 are objected to because of the following informalities: the acronym "GAS" while being properly defined in the specification is not defined in the claims, the examiner suggest simply adding the definition "Gas Anti-Solvent" before GAS in at least the first instance of the acronym claim 18. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 recites the limitation "(NHS)" in line 1. There is insufficient antecedent basis for this limitation in the claim. The examiner reminds the applicant that a genus defined in an earlier claim does not define the species in a dependent claim. To expedite the examining process the examiner will still search for a NHS functionalized PEG since this rejection can be overcome by amendment.

Claims 19 and 25 contain the trademark/trade name Nektar™ SCF. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of **35 U.S.C. 112**, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or

trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a supercritical fluid technique known as SCF or SEDS and, accordingly, the identification/description is indefinite. To expedite the examining process the examiner will interpret the claims in which the particulate has been formed using SCF or SEDS as defined in the specification.

Claims 30 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically claim 30 claims a MW for the composition, a composition generally describes a mixture of compounds therefore it would be impossible for a composition to have a MW, to expedite the examining process the examiner will search for a PAG polymer within the cited weight range. Regarding claim 37 it is not known what is meant by "reduction of particle size of the target substance to 70% or less of that of the starting material", particularly what is encompassed by starting material and is therefore considered to be indefinite by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8,17-20,22-27 and 32-36,38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,372,260).

Anderson discloses incorporation of active substances (including proteins) in polymer carrier matrixes (can be comprised of polyethyleneoxide same as PEG) and the method to make the composition, which includes anti-solvent techniques such as GAS and SEDS. See abstract, col 3 lin 58-62, col 4 lin 4-5 and experimental section. Regarding the limitations on the solvent level the examiner considers these limitations met since it is obvious to the skilled artisan that particles prepared using the GAS technique will be substantially free of solvent. Also regarding the limitations of the size of the particles, the particle size in the experimental section is within applicants claimed range although none of the polymers are PEG, it is obvious however that since the polymers for use in Andersons patent are interchangeable with PEG polymers, particles made from PEG should provide a similar size as those disclosed in the experimental section. Besides the above the only limitation for the formation of the particles seems to be from latter dependent claims that the particles are formed by SCF or SEDS, since Anderson discloses the same polymer carrier as applicant (PEG) and the same technique to form the particles (SEDS) it is obvious that the particles formed in Anderson will be the same volume and mean volume range because the polymers and technique to form the particles is the same. Also it is obvious for the skilled artisan through routine experimentation to form particles within a desired volume and mean diameter spread for pharmaceutical powders to reach the desired consistency of the powder. Regarding the limitation on the amount of impurities in claim 7 this limitation is

considered to be met by the examiner since Anderson only discloses particles formed from commercially sourced proteins and polymers as representative examples and PEG is normally bought from commercial sources, the particles are considered by the examiner to be relatively free of solvent and therefore there are substantially no impurities in the composition. Regarding claims 20 and 38, from the experimental section there was no mention of subsequent evaporative air-drying after the particles were formed by SEDS, therefore the limitation is met. Regarding the limitations on pressure and temperature for the anti-solvent (CO_2), Anderson discloses the same anti-solvent used in the SEDS procedure, the temperature and pressure used for the anti-solvent was given no patentable weight by the examiner because the inventive entity of the applicants claimed invention is the supercritical fluid technique of SEDS, CO2 is the anti-solvent as long as it is at the supercritical phase modifying the temperature or pressure will not change the technique to form the particles. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

Claims 1-8,17-20,22-27 and 32-36,38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandel et al. (WO 02/20624 A1, cited by applicant).

Mandel discloses controlled release pharmaceuticals prepared by supercritical fluid processing techniques. See abstract. The pharmaceuticals are comprised of a biologically active agent (including proteins) and a polymer such as PEG. See claims and examples. The anti-solvent is CO2 which is within the temperature and pressure cited by applicants. Regarding the limitation that the composition has a low or undetectable residual solvent is met because in the examples Mandel does only reacts the polymer, active ingredient and CO_2. It is assumed by the examiner that since the polymers used to create the particles and the technique is the same the particle size will also be the same, the burden is shifted to applicants to show that the particles disclosed in Mandel would not satisfy the limitations of particle size and volume mean diameter spread. Regarding the limitation on the amount of impurities in claim 7 this limitation is considered to be met by the examiner since Mandel only discloses particles formed from commercially sourced enzymes and polymers as representative examples and PEG is normally bought from commercial sources, the particles are considered by the examiner to be free of solvent and therefore there are substantially no impurities in the composition. Regarding claims 20 and 38, from the examples there was no mention of subsequent evaporative air-drying after the particles were formed by SEDS, therefore the limitation is met.

Claims 1-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,372,260) in view of Mandel et al. (WO 02/20624 A1, cited by applicant) in view of Harris (US 6,258,351 B1).

Anderson is disclosed above. Anderson discloses incorporation of active substances in carrier matrixes to form particles using SEDS but is silent on covalent attachment of the actives to the carrier (such as PEG) and functional groups attached to the carrier such as NHS. Anderson is also silent on exact temperature and pressure of the anti-solvent CO_2.

Mandel is disclosed above and is used to primarily show that the supercritical fluid techniques used CO_2 within applicants claimed temperature and pressure range.

Harris is used only to show that it was well known in the art at the time of the invention that PEG could be functionalized with NHS and capable of binding through reaction of the functional groups to biologically active agents (including proteins). See examples and claims. Regarding the solubility of the active substance, it is assumed by the examiner that at least some of the actives encompassed within Anderson, Mandel and Harris would fall within applicants claim that the actives have low solubility of at least 300 mg/ml, the burden is shifted to the applicants to show that none of the actives encompassed within the three patents would not have low aqueous solubility or a solubility in mg/ml within applicants claimed range. Regarding claim 16 by combining Anderson, Mandel and Harris one would particulate PEGylated actives by SEDS, the same technique as applicants, therefore it is obvious that the activity of the active (protein) would by the same since the same technique to particulate the same

compound will retain the same activity. Regarding claim 30 Harris discloses PEG within applicants claimed MW range, see claim 18. Regarding claim 31 since the PEG conjugated to the actives encompassed within Harris are the same as applicants claimed invention the examiner assumes they are the same PEGylated actives and would therefore have the same melting point, since the examiner assumes applicants claimed PEGylated actives would meet this limitation then it is obvious that Harris would also meet this limitation. Besides the above In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) and In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) from the above arguments apply. Regarding claim 37 by combining the teachings of Harris who discloses the same PEGylated actives as applicant with Anderson and Mandel who disclose the same super critical fluid technique to particulate the composition it is obvious that the target molecule disclosed in Harris would be reduced in volume 70% when compared to the starting material by applying the SEDS technique, because the same polymer will be reduced to the same volume when applying the same technique to particulate.

It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because Anderson discloses all of applicants claimed invention except for PEGylated active ingredients and the exact temperature and pressure of the anti-solvent while Mandel showed the temperature and pressure of the anti-solvent as claimed were well known to be used in super-critical fluid techniques at the time of the invention and Harris was used to show that PEG functionalized with NHS and capable of binding to

biologically active agents was well known in the art at the time of the invention The motivation to combine the above documents would be a pharmaceutical formation comprised of submicron particles containing PEGylated bioactive agents, the particles formed by the super critical fluid technique SEDS, with the advantage of providing poorly soluble or insoluble compounds with biological activity. Thus, the claimed invention, taken as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James W. Rogers, Ph.D. whose telephone number is (571) 272-7838. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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